

Old Claim No.	New Claim No.	Previous Status	Revised New Claim No.
88	178	allowed	181/182
89	179	allowed	187
90	180	allowed	None
94	182	allowed	202
117	184		178
118	185	allowed	179
119	186	allowed	None
120	187	allowed	180
121	188		None
122	189		181/182
123	190		184
124	191	allowed	183
126	192		185
127	195		185/188
128	196		189
129	197		190
130	198		191
131	199		192
132	200		193
133	201		197
134	202		198
135	203	allowed	199
137	193	allowed	186
138	204	allowed	194
139	205	allowed	None
140	206	allowed	195
142	207	allowed	None
143	208		205
144	209		206
145	210		207
146	211		208

Old Claim No.	New Claim No.	Previous Status	Revised New Claim No.	Added Claims (This Amdt.)
147	212		209	
148	213		210	
149	214		None	
150	215	allowed	220	
151	216	allowed	187/221	
152	221	allowed	202	
153	225		212	
154	217	allowed	222	
155	218	allowed	223	
156	219	allowed	224	
157	220	allowed	225	
158	cancel	cancel		
159	229	allowed	200	
160	230	allowed	201	
165	231	allowed	216	
166	232	allowed	217	
167	233	allowed	218	
168	234	allowed	219	
169	222	allowed	None	
170	223	allowed	None	
171	224	allowed	211	
172	226		213	
173	227		214	
174	228		215	
175	181	allowed	None	
176	183	allowed	203	
177	194	allowed	204	
				226
				227
				228

Please cancel claims 88-90, 94, 117-135, 137-140, 142-160, 165-177, without prejudice, and replace them with the new claims provided below.

178. A purified and isolated nucleic acid encoding a glial cell line-derived neurotrophic factor (GDNF) polypeptide, wherein said nucleic acid:

- (a) comprises nucleotides 304 through 705 of SEQ ID NO:3 or nucleotides 105 through 506 of SEQ ID NO:5; or
- (b) encodes a polypeptide comprising the GDNF polypeptide set forth in SEQ ID NO:4 or SEQ ID NO:6; or
- (c) hybridizes to an oligonucleotide probe fully complementary to a nucleic acid encoding the polypeptide of SEQ. ID. NO:6 under hybridization conditions comprising 6X SSPE and 0.1% SDS at 50°C, followed by washing in 2X SSPE and 0.1% SDS at room temperature and twice in 0.1x SSPE, 0.1% SDS preheated to 50°C, and wherein said GDNF polypeptide has the capability to promote dopamine uptake in dopaminergic neurons; or
- (d) hybridizes to an oligonucleotide probe fully complementary to a nucleic acid encoding amino acids 2 to 86 of SEQ ID NO:4 under hybridization conditions comprising 6X SSPE, 0.1% SDS and 30% formamide at 42°C, followed by washing in 2X SSPE and 0.1% SDS at room temperature and twice in 0.1x SSPE, 0.1% SDS preheated to 50°C, and wherein said GDNF polypeptide has the capability to promote dopamine uptake in dopaminergic neurons.

179. The nucleic acid of claim 178 comprising nucleotides 105 through 506 of SEQ ID NO:5, and wherein said GDNF polypeptide has the capability to promote dopamine uptake in dopaminergic neurons.

180. The nucleic acid of claim 178 wherein said nucleic acid encodes a polypeptide comprising the GDNF polypeptide set forth in SEQ ID NO:4 or SEQ ID NO:6 and wherein said GDNF polypeptide has the capability to promote dopamine uptake in dopaminergic neurons.

181. The nucleic acid of claim 178 wherein said nucleic acid additionally encodes for an amino-terminal methionine residue when said GDNF polypeptide is recombinantly produced by a bacterial expression system.

182. The nucleic acid of claim 179 or 180 wherein said nucleic acid additionally encodes for an amino-terminal methionine residue when said GDNF polypeptide is recombinantly produced by a bacterial expression system.

183. A purified and isolated nucleic acid encoding a polypeptide comprising the GDNF pre-pro polypeptide set forth in SEQ ID NO:27 or SEQ ID NO:28.

184. A purified and isolated nucleic acid comprising a nucleic acid fully complementary to the nucleic acid of claim 178, 179, 180, 181, 182, or 183.

185. An expression vector comprising the nucleic acid of claim 178, 179, 180, 181, or 183.

186. An expression vector comprising the nucleic acid of claim 179 or 180.

187. An expression vector comprising the nucleic acid of claim 182.

188. An isolated host cell comprising the expression vector of claim 185 and wherein said cell is capable of producing said GDNF polypeptide.

189. The host cell of claim 185 wherein said cell is an animal cell.

190. The host cell of claim 185 wherein said cell is a COS cell.

191. The host cell according to claim 185 wherein said cell is a microorganism.

192. The host cell of claim 185 wherein said cell is a bacterial cell.

193. The host cell of claim 185 wherein said cell is *E. coli*.

194. An isolated host cell comprising the expression vector of claim 186 wherein said cell is capable of producing said GDNF polypeptide

195. The host cell of claim 194 wherein said cell is an animal cell.

196. The host cell according to claim 194 wherein said cell is an *E. coli* cell.

197. The host cell according to claim 188 wherein said cell is transformed or transfected *ex vivo* and wherein said cell expresses and secretes said GDNF polypeptide.

198. The host cell according to claim 188 wherein said cell is suitable for human implantation and wherein said cell expresses and secretes said GDNF polypeptide.

199. An isolated host cell which expresses a nucleic acid encoding a GDNF polypeptide, wherein said nucleic acid is operatively linked to a non-native promoter and wherein said nucleic acid:

(a) comprises nucleotides 105 through 506 of SEQ ID NO:5, or

(b) encodes a polypeptide comprising the GDNF polypeptide of SEQ ID NO:6.

200. An isolated host cell which expresses a nucleic acid encoding a GDNF polypeptide, wherein said nucleic acid comprises nucleotides 105 through 506 of SEQ ID NO:5 operatively linked to a non-native promoter; and wherein said GDNF polypeptide has the capability to promote dopamine uptake in dopaminergic neurons.

201. An isolated host cell which expresses a nucleic acid encoding a polypeptide comprising the GDNF polypeptide set forth in SEQ ID NO:4 or SEQ ID NO:6, wherein said nucleic acid is operatively linked to a non-native promoter, and wherein said GDNF polypeptide has the capability to promote dopamine uptake in dopaminergic neurons.

202. A method for the bacterial production of a GDNF polypeptide comprising the steps of:

- (a) culturing the host cell comprising the vector of claim 187;
- (b) maintaining said host cell under conditions allowing the expression of said GDNF polypeptide by said host cell; and optionally,
- (c) isolating said GDNF polypeptide produced by said cell.

203. The method according to claim 202 wherein said host cell is *E. coli*.

204. A method for the production of a GDNF polypeptide comprising the steps of:

- (a) culturing a host cell transformed or transfected with the vector of claim 186 under conditions suitable for the expression of said GDNF polypeptide; and optionally
- (b) isolating said GDNF polypeptide produced by said cell.

205. A method for the production of a GDNF polypeptide comprising the steps of:

- (a) culturing a host cell transformed or transfected with the vector of claim 185 under conditions suitable for the expression of said GDNF polypeptide; and optionally
- (b) isolating said GDNF polypeptide produced by said host cell.

206. The method according to claim 205 wherein said cell is an animal cell.

207. The method according to claim 206 wherein said cell is a COS cell.

208. The method according to claim 204 wherein said cell is a microorganism.

209. The method according to claim 208 wherein said cell is *E. coli*.

210. The method according to claim 204 further comprising a step of refolding said GDNF polypeptide.

211. The method according to claim 202 further comprising a step of refolding said GDNF polypeptide to form a disulfide-bonded dimer.

212. A method for the production of a GDNF polypeptide, comprising the steps of:
- (a) culturing a transformed or transfected host cell comprising a nucleic acid encoding said GDNF polypeptide under conditions suitable for the expression of said GDNF polypeptide, wherein said nucleic acid is operatively linked to a non-native promoter, and wherein said nucleic acid encodes said GDNF polypeptide having the capability to promote dopamine uptake in dopaminergic neurons and
 - (i) hybridizes to an oligonucleotide probe fully complementary to a nucleic acid encoding a polypeptide of SEQ. ID. NO:6 under hybridization conditions comprising 6X SSPE and 0.1% SDS at 50°C, followed by washing in 2X SSPE and 0.1% SDS at room temperature and twice in 0.1x SSPE, 0.1% SDS preheated to 50°C; or
 - (ii) hybridizes to an oligonucleotide probe fully complementary to a nucleic acid encoding amino acids 2 to 86 of SEQ ID NO:4 under hybridization conditions comprising 6X SSPE, 0.1% SDS and 30% formamide at 42°C, followed by washing in 2X SSPE and 0.1% SDS at room temperature and twice in 0.1x SSPE, 0.1% SDS preheated to 50°C; and
 - (b) isolating said GDNF polypeptide produced in a substantially purified form from said host cell culture.
213. The method according to claim 212 wherein said host cell is an animal cell or microorganism.
214. The method according to claim 212 wherein the GDNF polypeptide produced is secreted by said host cell.
215. The method according to claim 212 further comprising a step of refolding the GDNF polypeptide produced to form a disulfide-bonded dimer.
216. A method for the production of a GDNF polypeptide, comprising the steps of:
- (a) culturing a transformed or transfected host cell comprising a nucleic acid encoding said GDNF polypeptide under conditions suitable for the expression of said GDNF

polypeptide, wherein said nucleic acid is operatively linked to a non-native promoter, and wherein said nucleic acid comprises nucleotides 105 through 506 of SEQ ID NO:5; and

- (b) isolating said GDNF polypeptide in a substantially purified form from said host cell culture, and wherein said GDNF polypeptide has the capability to promote dopamine uptake in dopaminergic neurons.

217. The method according to claim 216 wherein said cell is an animal cell or microorganism.

218. The method according to claim 216 wherein the GDNF polypeptide produced by said host is secreted by said host cell.

219. The method according to claim 216 further comprising a step of refolding said GDNF polypeptide to form a disulfide-bonded dimer.

220. A method for the production of a GDNF polypeptide comprising the steps of:

- (a) culturing a transformed or transfected host cell comprising a nucleic acid encoding said GDNF polypeptide under conditions suitable for the expression of said polypeptide, wherein said nucleic acid sequence is operatively linked to a non-native promoter, and wherein said nucleic acid is selected from the group consisting of:
 - (i) nucleotides 304 through 705 of SEQ ID NO:3 or nucleotides 105 through 506 of SEQ ID NO:5; or
 - (ii) nucleotides encoding a polypeptide comprising an amino acid sequence set forth in SEQ ID NO:4 or SEQ ID NO:6; and
- (b) isolating said GDNF polypeptide produced in a substantially purified form from said host cell culture.

221. The method according to claim 220 wherein said nucleic acid further comprises a codon encoding an amino-terminal methionine residue when said GDNF polypeptide is recombinantly produced by a bacterial expression system.

222. The method according to claim 220 wherein said host cell is an animal cell or microorganism.